

AMENDMENTS TO THE TITLE

Please replace the title of the application with the following new title:

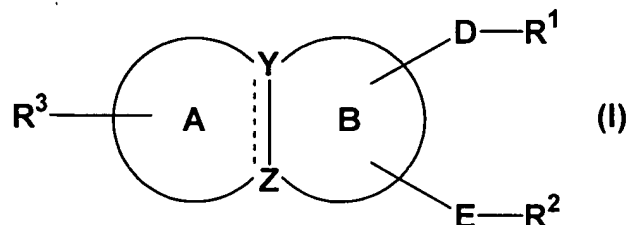
--CARBOXYLIC ACID DERIVED BENZOXAZINES AS AGENTS FOR THE
TREATMENT OF RESPIRATORY DISEASES--

AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph on page 5/269, line 22, through page 13/269, line 20, as follows:

That is, the present invention relates to

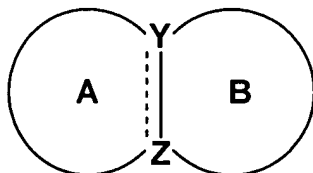
[1] a compound of formula (I)



[wherein R¹ and R² are each independently, an acidic group which may be protected, D and E are each independently, a bond or a spacer consisting of 1-8 ~~of atom~~atom(s) in the main chain, R³ is a substituent, ring A is a cyclic group which may have more substituent(s), ring B is a cyclic group which may have more substituent(s), Y and Z are each independently, a carbon atom or a nitrogen atom, and

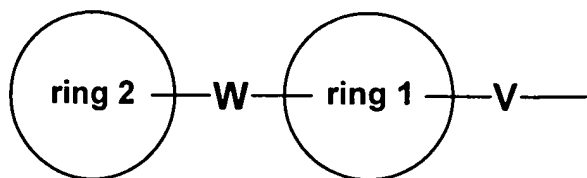
is a single bond or a double bond (provided that Y and/or Z is/are nitrogen atom(s), the bond is a single ~~bond~~bond), an N-oxide thereof, a salt thereof, a solvate thereof or a prodrug thereof,

[2] the compound according to the above [1], wherein



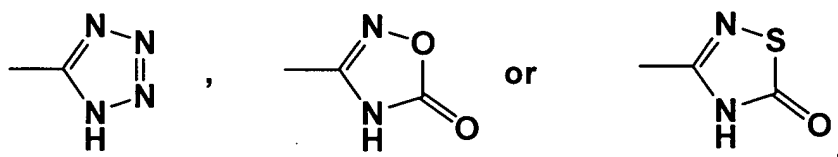
is 3,4-dihydro-2H-1,4-benzoxazine, 3,4-dihydro-2H-1,4-benzothiazine, 1,2,3,4-tetrahydroquinoxaline, 1,2,3,4-tetrahydroquinoline, 1,2-dihydroquinoline, 4H-1,4-benzoxazine, 4H-1,4-benzothiazine, quinoline, isoquinoline, quinoxaline, 1,2,3,4-tetrahydroisoquinoline, cinnoline, phthalazine, 4(1H)-quinolinone, 3,4-dihydro-2(1H)-quinolinone, 2(1H)-quinolinone, 1H-indole or indoline ring,

[3] the compound according to the above [1], wherein R³ is

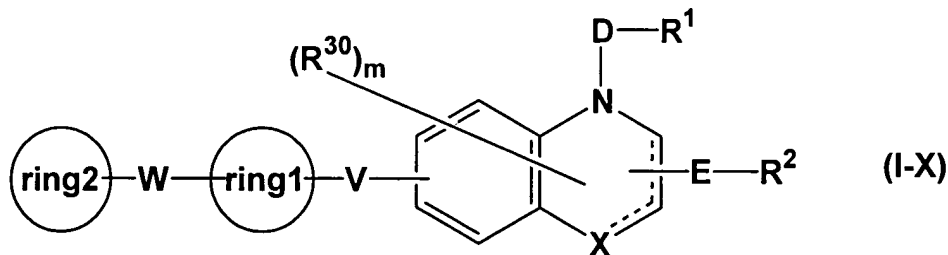


(wherein ring 1 is a cyclic group which may have substituent(s), V is a bond or a spacer having 1-8 ~~of atom~~atom(s) in the main chain, ~~ring 2~~ring 2 is a cyclic group which may have substituent(s), and W is a bond or a spacer having 1-8 ~~of atom~~atom(s) in the main chain),

[4] the compound according to the above [1], wherein the acidic group represented by R¹ and R² are each independently, -COOR^A (wherein R^A is hydrogen or C1-8 alkyl), -CONR^BSO₂R^C (wherein R^B is hydrogen or C1-8 alkyl, R^C is C1-8 hydrocarbon), -SO₂NR^BCOR^C (wherein all symbols have the same meaning as described hereinbefore),



[5] the compound according to the above [1], which is a compound of formula (I-X)



(wherein R³⁰ is hydrogen or a substituent, m is 0 or an integer of 1 to 4, L is a nitrogen atom, an oxygen atom, a sulfur atom which may be oxidized, a carbon atom or a bond, and the other symbols have the same meanings as in claims 1 and 3, and the adjacent two ~~time~~time bonds do not represent a double bond at the same ~~time~~time),

[6] the compound according to the above [3] or [5], wherein V is a divalent group comprising the combination of 1-4 member(s) selected from -CH₂- optionally having 1-2 ~~of substituent~~substituent(s), -CH=CH- optionally having 1-2 ~~of substituent~~substituent(s), -C≡C-, -NH- optionally having a substituent, -CO-, -O-, -S-, -SO- and SO₂-,

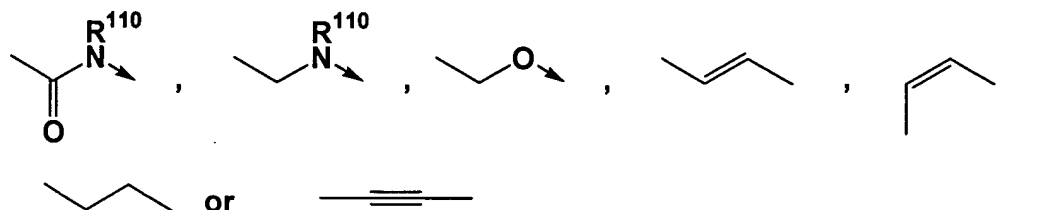
[6] the compound according to the above [3] or [5], wherein V is a divalent group comprising the combination of 1-4 member(s) selected from -CH₂- optionally having 1-2 ~~of substituent~~substituent(s), -CH=CH- optionally having 1-2 ~~of substituent~~substituent(s), -C≡C- ~~substituent(s)~~substituent(s),

$-\text{C}\equiv\text{C}-$, $-\text{NH}-$ optionally having a substituent, $-\text{CO}-$, $-\text{O}-$, $-\text{S}-$, $-\text{SO}-$ and SO_2- ,

[7] the compound according to the above [3] or [5], wherein $-\text{D}-\text{R}^1$ is $-\text{CO}-(\text{CH}_2)_2-\text{R}^1$, $-\text{CO}-(\text{CH}_2)_3-\text{R}^1$, $-\text{CO}-(\text{CH}_2)_4-\text{R}^1$ or C1-4 alkylene- R^1 ,

[8] the compound according to the above [3] or [5], wherein E is a bond or C1-4 alkylene,

[9] the compound according to the above [3] or [5] wherein V is



[10] the compound according to the above [1], which is selected from

- (1) 4-(3-carboxypropyl)-8-((4-(4-phenylbutoxy)benzoyl)amino)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (2) 4-(3-carboxypropyl)-8-((2E)-3-[4-(4-phenylbutyl)phenyl]-2-propenoyl)amino)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (3) 4-[8-{{4-(4-phenylbutoxy)benzoyl}amino}-2-(1H-tetrazol-5-yl)-2,3-dihydro-4H-1,4-benzoxazin-4-yl]butanoic acid,
- (4) 4-(3-carboxypropyl)-8-{{4-(4-phenylbutoxy)benzyl}amino}-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (5) 4-(3-carboxypropyl)-8-{{(E)-2-[4-(4-phenylbutoxy)phenyl]vinyl}-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (6) 4-(3-carboxypropyl)-8-{{2-[4-(4-phenylbutoxy)phenyl]ethyl}-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (7) (2S)-4-(3-carboxypropyl)-8-{{4-(4-phenylbutoxy)benzoyl}amino}-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (8) (2R)-4-(3-carboxypropyl)-8-{{4-(4-phenylbutoxy)benzoyl}amino}-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (9) 4-(3-carboxypropyl)-8-{{4-[2-(2,3-dihydro-1H-inden-2-yl)ethoxy]benzoyl}amino)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (10) 4-(3-carboxypropyl)-8-{{4-[(5-phenylpentyl)oxy]benzoyl}amino)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,

- (11) 4-(3-carboxypropyl)-8-({4-[(7-phenylheptyl)oxy]benzoyl}amino)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (12) 4-(3-carboxypropyl)-8-({4-[(4-methylpentyl)oxy]benzoyl}amino)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (13) 4-(3-carboxypropyl)-8-{[4-(4-phenoxybutoxy)benzoyl]amino}-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (14) 4-(3-carboxypropyl)-8-({4-[3-(2,3-dihydro-1H-inden-2-yl)propoxy]benzoyl}amino)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (15) 4-(3-carboxypropyl)-8-({4-[4-(4-fluorophenyl)butoxy]benzoyl}amino)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (16) 4-(3-carboxypropyl)-8-({4-[4-(2-methylphenoxy)butoxy]benzoyl}amino)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (17) 4-(3-carboxypropyl)-8-({4-[4-(2-fluorophenoxy)butoxy]benzoyl}amino)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (18) 4-(3-carboxypropyl)-8-({4-[4-(2-chlorophenoxy)butoxy]benzoyl}amino)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (19) 4-(3-carboxypropyl)-8-[(4-{4-[2-(trifluoromethyl)phenoxy]butoxy}benzoyl)amino]-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (20) 4-(3-carboxypropyl)-8-({4-[3-(2-methylphenoxy)propoxy]benzoyl}amino)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (21) 4-(2-({[(4-methylphenyl)sulfonyl]amino}carbonyl)-8-{[4-(4-phenylbutoxy)benzoyl]amino}-2,3-dihydro-4H-1,4-benzoxazin-4-yl)butanoic acid,
- (22) 4-(2-({[(methylsulfonyl)amino]carbonyl}-8-{[4-(4-phenylbutoxy)benzoyl]amino}-2,3-dihydro-4H-1,4-benzoxazin-4-yl)butanoic acid,
- (23) 4-(2-({[(benzylsulfonyl)amino]carbonyl}-8-{[4-(4-phenylbutoxy)benzoyl]amino}-2,3-dihydro-4H-1,4-benzoxazin-4-yl)butanoic acid,
- (24) 4-(3-carboxypropyl)-8-{(E)-2-[4-(4-phenoxybutoxy)phenyl]vinyl}-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (25) 4-(3-carboxypropyl)-8-{(E)-2-[4-(2,3-dihydro-1H-inden-2-ylmethoxy)phenyl]vinyl}-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,

- (26) 4-(3-carboxypropyl)-8-((E)-2-{4-[3-(2,3-dihydro-1H-inden-2-yl)propoxy]phenyl} vinyl)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (27) 4-(3-carboxypropyl)-8-((E)-2-{4-[(5-phenoxypropyl)oxy]phenyl} vinyl)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (28) 4-(3-carboxypropyl)-8-((E)-2-{4-[4-(4-methoxyphenoxy)butoxy]phenyl} vinyl)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (29) 4-(3-carboxypropyl)-8-((E)-2-{4-[3-(4-fluorophenoxy)propoxy]phenyl} vinyl)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (30) 4-(3-carboxypropyl)-8-((E)-2-[4-(3-phenoxypropoxy)phenyl] vinyl)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (31) 4-(3-carboxypropyl)-8-((E)-2-{4-[3-(2-chlorophenoxy)propoxy]phenyl} vinyl)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (32) 4-(3-carboxypropyl)-8-{2-[4-(4-phenoxybutoxy)phenyl]ethyl}-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,
- (33) 4-[8-{2-[4-(4-phenylbutoxy)phenyl]ethyl}-2-(1H-tetrazol-5-yl)-2,3-dihydro-4H-1,4-benzoxazin-4-yl]butanoic acid,
- (34) 4-[8-{(E)-2-[4-(4-phenylbutoxy)phenyl]vinyl}-2-(1H-tetrazol-5-yl)-2,3-dihydro-4H-1,4-benzoxazin-4-yl]butanoic acid,
- (35) 4-(2-(5-oxo-4,5-dihydro-1,2,4-thiadiazol-3-yl)-8-{[4-(4-phenylbutoxy)benzoyl]amino}-2,3-dihydro-4H-1,4-benzoxazin-4-yl)butanoic acid,
- (36) 4-(2-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)-8-{(E)-2-[4-(4-phenylbutoxy)phenyl]vinyl}-2,3-dihydro-4H-1,4-benzoxazin-4-yl)butanoic acid,
- (37) 4-oxo-4-(8-((4-(4-phenylbutoxy)benzoyl)amino)-2-(1H-tetrazol-5-yl)-2,3-dihydro-4H-1,4-benzoxazin-4-yl)butanoic acid, and
- (38) 4-(3-carboxypropyl)-8-((4-(4-phenylbutoxy)benzyl)oxy)-3,4-dihydro-2H-1,4-benzoxazine-2-carboxylic acid,

[11] a pharmaceutical composition comprising the compound of formula (I) described in the above [1] or an N-oxide thereof, a salt thereof, a solvate thereof or a prodrug thereof,

[12] the pharmaceutical composition according to the above [11], which is an agent for the prevention and/or treatment of a disease mediated by cysLT₂,

[13] the pharmaceutical composition according to the above [12], wherein the disease mediated by cysLT₂ is a respiratory disease,

[14] the pharmaceutical composition according to the above [13], wherein the respiratory disease is asthma or chronic obstructive pulmonary disease,

[15] a medicine comprising the compound of formula (I) described in the above [1], an N-oxide thereof, a salt thereof, a solvate thereof or a prodrug thereof and one or more member(s) selected from a cysLT₁ receptor antagonist, a steroidal agent, an antihistamine agent, a phosphodiesterase 4 inhibitor, an elastase inhibitor, an anticholinergic agent and a sympathomimetic agent,

[16] a method for the prevention and/or treatment of the diseases mediated by cysLT₂ characterized by administering to a mammal an effective amount of the compound of formula (I) described in the above [1], an N-oxide thereof, a salt thereof, a solvate thereof or a prodrug thereof,

[17] a method for the prevention and/or treatment of the diseases mediated by cysLT₂ characterized by administering to a mammal an effective amount of the compound of formula (I) described in the above [1], an N-oxide thereof, a salt thereof, a solvate thereof or a prodrug thereof, in combination with a cysLT₁ receptor antagonist, a steroidal agent, an antihistamine agent, a phosphodiesterase 4 inhibitor, an elastase inhibitor, an anticholinergic agent ~~and~~ and/or a sympathomimetic drug and

[18] use of the compound of formula (I) described in the above [1], for the manufacture of an agent for the prevention and/or treatment of the disease mediated by cysLT₂.

Please amend the paragraph on page 13/269, lines 21-26, as follows:

In the present specification, the cyclic group in the cyclic group optionally having substituent(s) represented by ring A is, C3-15 carbocyclic ring, or 3-15 membered mono-, bi- or tri-cyclic partially or completely saturated aromatic heterocyclic ring comprising 1-5 ~~of hetero atom~~ hereto atom(s) selected from oxygen, nitrogen and/or sulfur.

Please amend the paragraph on page 14/269, line 20, through page 17/26, line 28, as follows:

In the present invention, the 3-15 membered mono-, bi- or tri-cyclic partially or completely saturated aromatic heterocyclic ring comprising 1-5 ~~of hetero atom~~ hereto atom(s) selected from oxygen, nitrogen and/or sulfur includes, e.g. pyrrole, imidazole, triazole, tetrazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, azepine, diazepine, furan, pyran, oxepin, thiophene,

thiopyran, thiepin, oxazole, isoxazole, thiazole, isothiazole, furazane, oxadiazole, oxazine, oxadiazine, oxazepine, oxadiazepine, thiadiazole, thiazine, thiadiazine, thiazepine, thiadiazepine, indole, isoindole, indolizine, benzofuran, isobenzofuran, benzothiophene, isobenzothiophene, dithianaphthalene, indazole, quinoline, isoquinoline, quinolizine, purine, phthalazine, pteridine, naphthyridine, quinoxaline, quinazoline, cinnoline, benzoxazole, benzothiazole, benzimidazole, chromene, benzoxepine, benzoxazepine, benzoxadiazepine, benzothiepine, benzothiazepine, benzothiadiazepine, benzazepine, benzodiazepine, benzofurazane, benzothiadiaazole, benzotriazole, carbazole, β -carboline, acridine, phenazine, dibenzofuran, xanthene, dibenzothiophene, phenothiazine, phenoxazine, phenoxathiin, thianthrene, phenanthridine, phenanthroline, perimidine, pyrazolopyridine, aziridine, azetidine, pyrroline, pyrrolidine, imidazoline, imidazolidine, triazoline, triazolidine, tetrazoline, tetrazolidine, pyrazoline, pyrazolidine, dihydropyridine, tetrahydropyridine, piperidine, dihydropyrazine, tetrahydropyrazine, piperazine, dihydropyrimidine, tetrahydropyrimidine, perhydropyrimidine, dihydropyridazine, tetrahydropyridazine, perhydropyridazine, dihydroazepine, tetrahydroazepine, perhydroazepine, dihydrodiazepine, tetrahydrodiazepine, perhydrodiazepine, oxirane, oxetane, dihydrofuran, tetrahydrofuran, dihydropyran, tetrahydropyran, dihydrooxepin, tetrahydrooxepin, perhydrooxepin, thiirane, thietane, dihydrothiophene, tetrahydrothiophene, dihydrothiopyran, tetrahydrothiopyran, dihydrothiepin, tetrahydrothiepin, perhydrothiepin, dihydrooxazole, tetrahydrooxazole (oxazolidine), dihydroisoxazole, tetrahydroisoxazole (isoxazolidine), dihydrothiazole, tetrahydrothiazole (thiazolidine), dihydroisothiazole, tetrahydroisothiazole (isothiazolidine), dihydrofurazane, tetrahydrofurazane, dihydrooxadiazole, tetrahydrooxadiazole (oxadiazolidine), dihydrooxazine, tetrahydrooxazine, dihydrooxadiazine, tetrahydrooxadiazine, dihydrooxazepine, tetrahydrooxazepine, perhydrooxazepine, dihydrooxadiazepine, tetrahydrooxadiazepine, perhydrooxadiazepine, dihydrothiadiazole, tetrahydrothiadiazole (thiadiazolidine), dihydrothiazine, tetrahydrothiazine, dihydrothiadiazine, tetrahydrothiadiazine, dihydrothiazepine, tetrahydrothiazepine, perhydrothiazepine, dihydrothiadiazepine, tetrahydrothiadiazepine, perhydrothiadiazepine, morpholine, thiomorpholine, oxathiane, indoline, isoindoline, dihydrobenzofuran, perhydrobenzofuran, dihydroisobenzofuran, perhydroisobenzofuran, dihydrobenzothiophene, perhydrobenzothiophene, dihydroisobenzothiophene, perhydroisobenzothiophene, dihydroindazole, perhydroindazole, dihydroquinoline,

tetrahydroquinoline, perhydroquinoline, dihydroisoquinoline, tetrahydroisoquinoline, perhydroisoquinoline, dihydrophthalazine, tetrahydrophthalazine, perhydrophthalazine, dihydronaphthyridine, tetrahydronaphthyridine, perhydronaphthyridine, dihydroquinoxaline, tetrahydroquinoxaline, perhydroquinoxaline, dihydroquinazoline, tetrahydroquinazoline, perhydroquinazoline, dihydrocinnoline, tetrahydrocinnoline, perhydrocinnoline, benzoxathiane, dihydrobenzoxazine, dihydrobenzothiazine, pyrazinomorpholine, dihydrobenzoxazole, perhydrobenzoxazole, dihydrobenzothiazole, perhydrobenzothiazole, dihydrobenzimidazole, perhydrobenzimidazole, dihydrobenzazepine, tetrahydrobenzazepine, dihydrobenzodiazepine, tetrahydrobenzodiazepine, benzodioxepane, dihydrobenzoxazepine, tetrahydrobenzoxazepine, dihydrocarbazole, tetrahydrocarbazole, perhydrocarbazole, dihydroacridine, tetrahydroacridine, perhydroacridine, dihydrodibenzofuran, dihydrodibenzothiophene, tetrahydrodibenzofuran, tetrahydrodibenzothiophene, perhydrodibenzofuran, perhydrodibenzothiophene, dioxolane, dioxane, dithiolane, dithiane, dioxaindan, benzodioxane, chroman, benzodithiolane, benzodithiane, azaspiro[4.4]nonane, oxazaspiro[4.4]nonane, dioxaspiro[4.4]nonane, azaspiro[4.5]decane, thiaspiro[4.5]decane, dithiaspiro[4.5]decane, dioxaspiro[4.5]decane, oxazaspiro[4.5]decane, azaspiro[5.5]undecane, oxaspiro[5.5]undecane, dioxaspiro[5.5]undecane, azabicyclo[2.2.1]heptane, oxabicyclo[2.2.1]heptane, azabicyclo[3.1.1]heptane, azabicyclo[3.2.1]octane, oxabicyclo[3.2.1]octane, azabicyclo[2.2.2]octane, diazabicyclo[2.2.2]octane, tetrahydro- β -carboline, hexahydroazepinoindole, oxazaspiro[2.5]octane, hexahydroazepinoindazole, hexahydropyrazolopyridoazepine, tetrahydropyrazoloisoquinoline or tetrahydropyrazolonaphthyridine ring, etc.

Please amend the paragraph on page 22/269, lines 20-26, as follows:

The heterocyclic ring in the "(5) heterocyclic ring which may have substituent(s)" as a substituent has the same meaning as the 3-15 membered mono-, bi- or tri-cyclic aromatic heterocyclic ring comprising 1-5 of hetero atom(s) selected from oxygen, nitrogen and/or sulfur which may be partially or completely saturated in the "cyclic group which may have substituent(s)" represented by ring A.

Please amend the paragraph on page 27/269, line 7, through 28/269, line 27, as follows:

As the substituent in the "hydrocarbon group which may have substituent(s)" includes, for example, (1) nitro, (2) hydroxy, (3) oxo, (4) thioxo, (5) cyano, (6) carbamoyl, (7) aminocarbonyl substituted by C1-8 hydrocarbon etc. such as N-butylaminocarbonyl, N-cyclohexylmethylaminocarbonyl, N-butyl-N-cyclohexylmethylaminocarbonyl, N-cyclohexylaminocarbonyl, phenylaminocarbonyl, (8) carboxy, (9) C1-4 alkoxy carbonyl such as methoxycarbonyl, ethoxycarbonyl, etc., (10) sulfo, (11) halogen such as fluorine, chlorine, bromine, iodine, etc., (12) C1-4 lower alkoxy such as methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, sec-butoxy, tert-butoxy, etc., (13) phenoxy, (14) halogenophenoxy such as o-, m- or p-chlorophenoxy, o-, m- or p-bromophenoxy, (15) C1-4 lower alkylthio such as methylthio, ethylthio, n-propylthio, isopropylthio, n-butylthio, tert-butylthio, etc., (16) phenylthio, (17) C1-4 lower alkylsulfinyl such as methylsulfinyl, ethylsulfinyl, etc., (18) C1-4 lower alkylsulfonyl such as methylsulfonyl, ethylsulfonyl, etc., (19) amino, (20) C1-6 lower acylamino such as acetylamino, propionylamino, etc., (21) primary or secondary amino substituted with hydrocarbon group such as methylamino, ethylamino, n-propylamino, isopropylamino, n-butylamino, dimethylamino, diethylamino, cyclohexylamino, 1-carbamoyl-2-cyclohexylethylamino, N-butyl-N-cyclohexylmethylamino, phenylamino (wherein this "hydrocarbon group" has the same meaning as the above "hydrocarbon group" and it may be substituted with oxo, amino, carbamoyl, etc.), (22) C1-4 lower acyl such as formyl, acetyl, etc., (23) benzoyl, (24) a 5-6 membered heterocyclic ring comprising 1-4 hetero ~~atom~~ atom(s) selected from oxygen, sulfur, nitrogen, etc. besides carbon atom which may have 1-4 of ~~substituent~~ substituent(s) selected from 1-4 of substituent(s) selected from (a) halogen such as bromine, chlorine, fluorine, etc., (b) hydrocarbon group such as methyl, ethyl, propyl, isopropyl, benzyl, cyclohexyl, cyclohexylmethyl, cyclohexylethyl which may be substituted with oxo, hydroxy, etc., wherein the "hydrocarbon group" as the same meaning as the above "hydrocarbon group", (c) halogenophenoxy such as o-, m- or p-chlorophenoxy, o-, m- or p-bromophenoxy, etc., and (d) oxo, etc., for example, 2- or 3-thienyl, 2- or 3-furyl, 3-, 4- or 5-pyrazolyl, 4-tetrahydropyranyl, 2-, 4- or 5-thiazolyl, 3-, 4- or 5-isothiazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 2-, 4- or 5-imidazolyl, 1,2,3- or 1,2,4-triazolyl, 1H- or 2H-tetrazolyl, 2-, 3- or 4-pyridyl, 2-, 4- or 5-pyrimidyl, 3- or 4-pyridazinyl, quinolyl, isoquinolyl, indolyl, etc., (25) C1-10 haloalkyl such as difluoromethyl, trifluoromethyl, trifluoroethyl, trichloroethyl, etc., (26)

hydroxyimino, or (27) alkyloxyimino such as methyloxyimino, ethyloxyimino, etc.

Please amend the paragraph on page 28/269, line 28, through page 29/269, line 7, as follows:

The "hydrocarbon group which may have substituent(s)" may have 1-5 of substituent(s) selected from the above (1) to (27) and, when the "hydrocarbon group" is cycloalkyl, cycloalkenyl, aryl or aralkyl, it may have 1 to 4 of lower alkyl(s) having 1-4 carbon atoms such as methyl, ethyl, propyl, isopropyl, butyl, etc. as substituent(s), and also when it has more than one substituents, the substituents may be the same or different.

Please amend the paragraph on page 29/269, line 24, through page 30/269, line 15, as follows:

In the present specification, the "spacer consisting of 1-8 of atom in the main chain" represented by D and E means an interval of 1-8 of atom in succession. Here the "atom in the main chain" is counted so as to minimize the atom in the main chain. Here the "spacer consisting of 1-8 of atom(s) in the main chain" includes, for example, a divalent radical consisting of 1-8 member(s) selected from -CH₂- which may have 1-2 substituent(s), -CH=CH- which may have 1-2 substituent(s), -C≡C-, -NH- which may have a substituent, -CO-, -O-, -S-, -SO-, -SO₂-. Here the substituent of the methylene and the nitrogen atom has the same meaning as the "substituent" in the cyclic ring which may have a substituent represented by the above ring A, concretely, e.g. -CR¹⁰¹R¹⁰²-, -(CR¹⁰¹R¹⁰²)₂-, -(CR¹⁰¹R¹⁰²)₃-, -(CR¹⁰¹R¹⁰²)₄-, -CO(CR¹⁰¹R¹⁰²)₂-, -CO(CR¹⁰¹R¹⁰²)₃-, -CO(CR¹⁰¹R¹⁰²)₄-, -NR¹⁰³-, -CO-, -O-, -S-, -NR¹⁰³CO-, -CONR¹⁰³-, -NR¹⁰³COCR¹⁰¹R¹⁰²-, -CONR¹⁰³CR¹⁰¹R¹⁰²-, -C(R¹⁰¹)=C(R¹⁰²)-, -C≡C- (wherein R¹⁰¹ to R¹⁰³ are, hydrogen atom or a substituent having the same meaning as the "substituent" in the cyclic group which may have substituent represented by the above ring A.)A), etc.

Please amend the paragraph on page 35/269, line 3, through page 36/269, line 19, as follows:

The ring B is preferably a C3-15 mono-cyclic aromatic carbocyclic ring, partially or completely saturated one thereof, or a 3-15 membered mono-cyclic aromatic heteroring comprising 1-5 of ~~hetero-atom~~hetero atom(s) selected from oxygen, nitrogen and/or sulfur which

may be partially or completely saturated, more preferably, a 3-8 membered mono-cyclic aromatic heteroring comprising 1-3 ~~of hetero-atom~~hetero atom(s) selected from oxygen, nitrogen and/or sulfur which may be partially or completely saturated, furthermore preferably, pyrrole, imidazole, triazole, tetrazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, azepine, diazepine, furan, pyran, oxepin, thiophene, thiopyran, thiepin, oxazole, isoxazole, thiazole, isothiazole, furazane, oxadiazole, oxazine, oxadiazine, oxazepine, oxadiazepine, thiadiazole, thiazine, thiadiazine, thiazepine, thiadiazepine, aziridine, azetidine, pyrroline, pyrrolidine, imidazoline, imidazolidine, triazoline, triazolidine, tetrazoline, tetrazolidine, pyrazoline, pyrazolidine, dihydropyridine, tetrahydropyridine, piperidine, dihydropyrazine, tetrahydropyrazine, piperazine, dihydropyrimidine, tetrahydropyrimidine, perhydropyrimidine, dihydropyridazine, tetrahydropyridazine, perhydropyridazine, dihydroazepine, tetrahydroazepine, perhydroazepine, dihydrodiazepine, tetrahydrodiazepine, perhydrodiazepine, oxirane, oxetane, dihydrofuran, tetrahydrofuran, dihydropyran, tetrahydropyran, dihydrooxepin, tetrahydrooxepin, perhydrooxepin, thiiran, thietane, dihydrothiophene, tetrahydrothiophene, dihydrothiopyran, tetrahydrothiopyran, dihydrothiepin, tetrahydrothiepin, perhydrothiepin, dihydrooxazole, tetrahydrooxazole (oxazolidine), dihydroisoxazole, tetrahydroisoxazole(isoxazolidine), dihydrothiazole, tetrahydrothiazole (thiazolidine), dihydroisothiazole, tetrahydroisothiazole (isothiazolidine), dihydrofurazane, tetrahydrofurazane, dihydrooxadiazole, tetrahydrooxadiazole (oxadiazolidine), dihydrooxazine, tetrahydrooxazine, dihydrooxadiazine, tetrahydrooxadiazine, dihydrooxazepine, tetrahydrooxazepine, perhydrooxazepine, dihydrooxadiazepine, tetrahydrooxadiazepine, perhydrooxadiazepine, dihydrothiadiazole, tetrahydrothiadiazole (thiadiazolidine), dihydrothiazine, tetrahydrothiazine, dihydrothiadiazine, tetrahydrothiadiazine, dihydrothiazepine, tetrahydrothiazepine, perhydrothiazepine, dihydrothiadiazepine, tetrahydrothiadiazepine, perhydrothiadiazepine, morpholine, thiomorpholine, oxathiane, dioxolane, dioxane, dithiolane or dithiane ring.

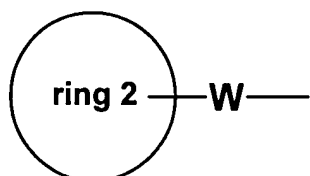
Please amend the paragraph on page 38/269, lines 18-25, as follows:

E is preferably a bond or a spacer consisting of 1-5 of atom in the main chain, more preferably, a divalent radical consisting of 1-5 members selected from a bond, -CH₂- which may have 1-2 ~~of~~-substituent(s), -NH- which may have a substituent, -CO-, -O-, -S-, -SO- and -SO₂-,

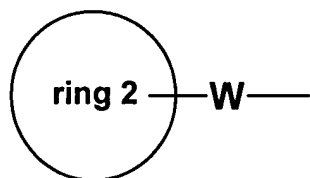
furthermore preferably, a bond, -CO-(CH₂)₂-, -CO-(CH₂)₃-, -CO-(CH₂)₄-, C1-4 alkylene (e.g. methylene, ethylene, propylene, butylene, etc.), particularly preferably a bond or C1-4 alkylene.

Please amend the paragraph on page 39/269, line 7, through page 40/269, line 19, as follows:

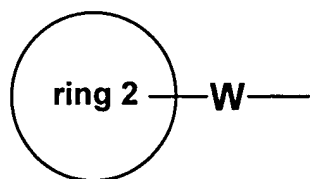
The substituent of ring 1 is preferably,



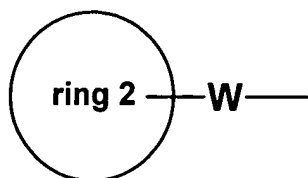
(wherein all symbols have the same meaning as described hereinbefore), hydroxy, halogen, nitro, amino, C5-10 carbocyclic ring, 5-10 membered heterocyclic ring, or C1-20 straight or branched alkyl, alkenyl or alkynyl in which optional 1-3 carbon atom(s) may be replaced by oxygen, sulfur, nitrogen, benzene ring, thiophene ring, C4-7 carbocyclic ring, carbonyl or carbonyloxy, and it may be further substituted with 1-3 of halogen, hydroxy, carboxy, azido or nitro, and more preferably,



(wherein all symbols have the same meaning as described hereinbefore), or C1-10 straight or branched alkyl, alkenyl or alkynyl in which optional 1-2 of the carbon atom(s) may be replaced by oxygen, sulfur, benzene ring, thiophene or C4-7 carbocyclic ring, and it may be further substituted by 1-2 of hydroxy, and more preferably,



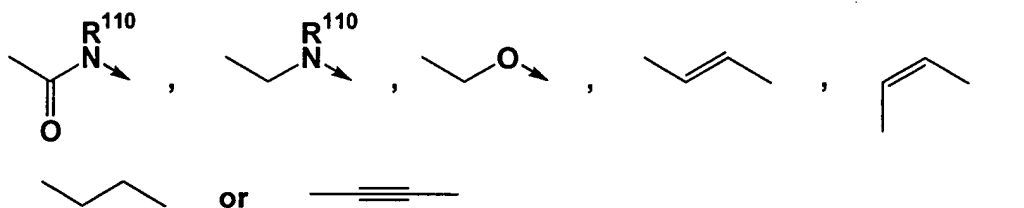
(wherein all symbols have the same meaning as described hereinbefore), or C1-10 straight or branched alkyl, alkenyl or alkynyl in which optional 1-2 of the carbon atom(s) may be replaced by oxygen, benzene ring, C5-7 carbocyclic ring, and most preferably,



(wherein all symbols have the same meaning as described hereinbefore), n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, n-nonyl, n-butyloxy, n-pentyloxy, n-hexyloxy, n-heptyloxy, n-octyloxy, n-nonyloxy, (2E)-2-pentenyl, (2E)-2-hexenyl, (2E)-2-heptenyl, (2E)-2-octenyl, (2E)-2-nonenyl, 7-octenyl, 2-octynyl, (2E)-2,7-octadienyl, 2-phenylethyl, 3-phenylpropyl, 4-phenylbutyl or 5-phenylpentyl.

Please amend the paragraphs on page 42/269, line 20, through page 43/269, line 16, as follows:

V is preferably, a bond or a spacer consisting of 1-5 of atom in the main chain, more preferably, a bond, a divalent radical consisting of 1-6 member(s) selected from -CH₂- optionally having 1-2 substituent(s), -CH=CH- optionally having 1-2 substituent(s), -C=C-C≡C-, -NH- optionally having a substituent, -CO-, -O-, -S-, -SO- and SO₂-, moreover preferably, -CONR¹⁰³-, -NR¹⁰³CO-, -CR¹⁰¹R¹⁰²NR¹⁰³-, -NR¹⁰³CR¹⁰¹R¹⁰²-, -NR¹⁰³COCR¹⁰¹R¹⁰²-, -CONR¹⁰³CR¹⁰¹R¹⁰²-, -O-CR¹⁰¹R¹⁰²-, -CR¹⁰¹R¹⁰²-O-, -NR¹⁰³COCR¹⁰¹=CR¹⁰²-, -CR¹⁰¹=CR¹⁰²CONR¹⁰³-, -NR¹⁰³-CR¹⁰¹R¹⁰²-, -CR¹⁰¹R¹⁰²-NR¹⁰³-, -(CR¹⁰¹R¹⁰²)₂-, -CR¹⁰¹=CR¹⁰²-, -C≡C- (wherein, R¹⁰¹ to R¹⁰³ are hydrogen or have the same meanings as the "substituent" in the cyclic group which may have substituent(s) represented by the above ring A), and specially preferably



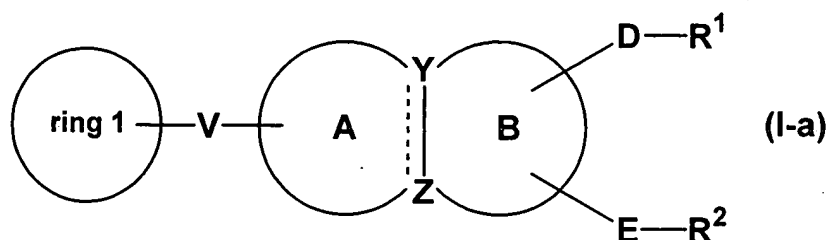
(wherein R¹¹⁰ is hydrogen or C1-8 alkyl, and the arrow means that it attaches to the ring A.)

W is preferably, a bond or a spacer consisting of 1-6 of atom(s) in the main chain, more preferably, a divalent radical consisting of 1-6 member(s) selected from a bond, -CH₂- optionally having 1-2 substituent(s), -NH- optionally having a substituent, -CO-, -O-, -S-, -SO-, -SO₂-, further preferably, -O-CH₂-, -O-(CH₂)₂-, -O-(CH₂)₃-, -O-(CH₂)₄-, -O-(CH₂)₅-, -CH₂-O-, -(CH₂)₂-O-, -(CH₂)₃-O-, -(CH₂)₄-O-, -(CH₂)₅-O-, -O-(CH₂)₃-O-, -O-(CH₂)₄-O-, -O-(CH₂)₅-O-, C1-6

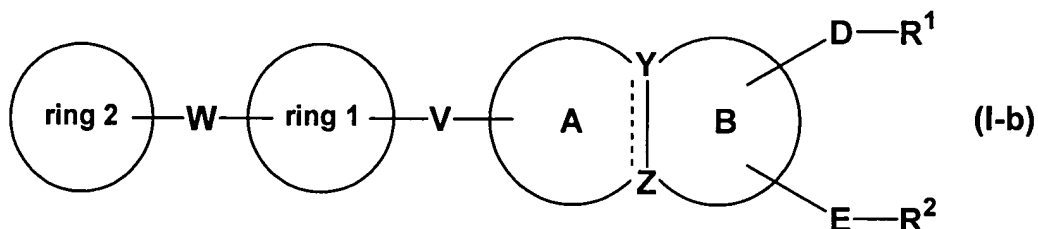
alkylene.

Please amend the paragraph on page 45/269, line 10, through page 46/269, line 8, as follows:

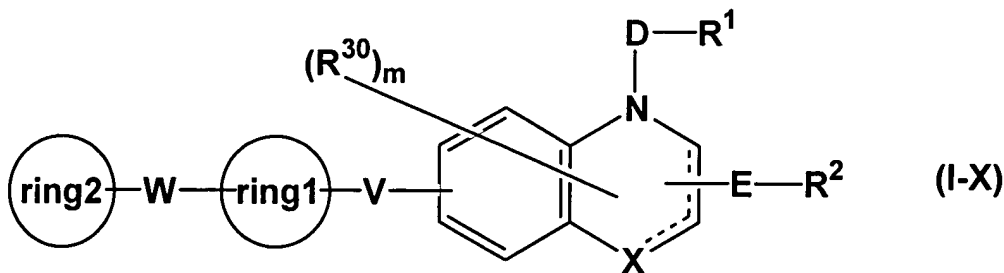
Among the compounds of formula (I), preferable compounds are, the compound of formula (I-a)



(wherein all symbols have the same meaning as described hereinbefore), more preferably, the compound of formula (I-b)



(wherein all symbols have the same meaning as described hereinbefore) and further preferably the compound of formula (I-X)



(wherein all symbols have the same meaning as described hereinbefore). In the formula (I-X), R^{30} is hydrogen or a substituent having the same meaning as the "substituent" in the "cyclic group optionally having substituent(s)" shown by the ring A. R^{30} is preferably hydrogen, hydroxy, C1-4 alkyl optionally substituted with 1-3 of halogen, C1-4 alkoxy, amino, nitro or halogen.